

SEQUENCE LISTING

<110> De Francesco, Raffaele
Tomei, Licia
Behrens, Sven-Erik

<120> METHOD FOR REPRODUCING IN VITRO THE
RNA-DEPENDENT RNA POLYMERASE AND TERMINAL NUCLEOTIDYL
TRANSFERASE ACTIVITIES ENCODED BY HEPATITIS C VIRUS (HCV)

<130> IT0002PCA

<150> 08/952,981
<151> 1998-03-23

<150> PCT/IT96/00106
<151> 1996-05-24

<150> RM95A000343
<151> 1995-05-25

<160> 14

<170> FastSEQ for Windows Version 4.0

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<213> Hepatitis C virus

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Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His Tyr
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Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala
65 70 75 80
Lys Leu Leu Ser Val Glu Ala Cys Lys Leu Thr Pro Pro His Ser
85 90 95
Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser
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Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu
115 120 125
Asp Thr Val Thr Pro Ile Asp Thr Thr Ile Met Ala Lys Asn Glu Val
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Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile
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Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
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Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser Tyr Gly
180 185 190
Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr Trp
195 200 205
Lys Ser Lys Lys Asn Pro Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe
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Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr
225 230 235 240

Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu
 245 250 255
 Thr Glu Arg Leu Tyr Ile Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln
 260 265 270
 Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser
 275 280 285
 Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg
 290 295 300
 Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu
 305 310 315 320
 Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu
 325 330 335
 Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp
 340 345 350
 Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser
 355 360 365
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 370 375 380
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 385 390 395 400
 Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala
 405 410 415
 Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His Phe Phe Ser Ile
 420 425 430
 Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr
 435 440 445
 Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu
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 485 490 495
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 <212> PRT
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 His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile
 50 55 60
 Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr
 65 70 75 80

Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly
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 Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala
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 Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala
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 Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu
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 Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val
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 Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr
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 Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro
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 Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser
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 Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser
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 Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly
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 Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala
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 Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp
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 Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg
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 Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val
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 Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val
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 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val
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 Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro
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 Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly
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 Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala
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 Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser Thr
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 Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn
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 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile
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Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp
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 Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr
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 Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val
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 Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp
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 Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser
 645 650 655
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 Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val
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 Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val
 770 775 780
 Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys
 785 790 795 800
 Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu
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 Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile
 820 825 830
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 Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr
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 Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp Leu Gly
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SEQUENCE LISTING

GENERAL INFORMATION

- (i) APPLICANT: ISTITUTO DI RICERCHE DI BIOLOGIA
MOLECOLARE P. ANGELETTI S.p.A.
- 5 (ii) TITLE OF INVENTION: METHOD FOR REPRODUCING
IN VITRO THE RNA-DEPENDENT RNA POLYMERASE
AND TERMINAL NUCLEOTIDYL TRANSFERASE
ACTIVITIES ENCODED BY HEPATITIS C VIRUS
(HCV)
- 10 (iii) NUMBER OF SEQUENCES: 14
- (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Societa Italiana Brevetti
(B) STREET: Piazza di Pietra, 39
(C) CITY: Rome
15 (D) COUNTRY: Italy
(E) POSTAL CODE: 1-00186
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk 3.5" 1.44
MBYTES
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS Rev. 6.22
(D) SOFTWARE: Microsoft Word 6.0
- 20 (viii) ATTORNEY INFORMATION
(A) NAME: DI CERBO, Mario (Dr.)
(C) REFERENCE: RM/X88530/PCT-DC
- 25 (ix) TELECOMMUNICATION INFORMATION
(A) TELEPHONE: 06/6785941
(B) TELEFAX: 06/6794692
(C) TELEX: 612287 ROPAT
- 30 (1) INFORMATION FOR SEQ ID NO: 1:
(i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 591 amino acids
(B) TYPE: amino acid
35 (C) STRANDEDNESS: single
(D) TOPOLOGY: linear
(ii) MOLECULE TYPE: protein

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(iii) HYPOTHETICAL: No
 (iv) ANTISENSE: No
 (v) FRAGMENT TYPE: C-terminal fragment
 (vi) ORIGINAL SOURCE:
 5 (A) ORGANISM: Hepatitis C Virus
 (C) ISOLATE : BK
 (vii) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4)
 described by Tomei et al. 1993
 (ix) FEATURE:
 10 (A) NAME: NS5B Non-structural polyprotein
 (C) IDENTIFICATION METHOD: Experimentally
 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:
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 20 25 30
 His His Asn Met Val Tyr Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg
 35 40 45
 Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu Asp Asp His Tyr
 20 50 55 60
 Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser Thr Val Lys Ala
 65 70 75 80
 Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr Pro Pro His Ser
 85 90 95
 25 Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser
 100 105 110
 Ser Lys Ala Val Asn His Ile His Ser Val Trp Lys Asp Leu Leu Glu
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 30 130 135 140
 Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile
 145 150 155 160
 Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys Met Ala Leu Tyr
 165 170 175
 35 Asp Val Val Ser Thr Leu Pro Gln Val Val Met Gly Ser Ser Tyr Gly
 180 185 190
 Phe Gln Tyr Ser Pro Gly Gln Arg Val Glu Phe Leu Val Asn Thr Trp

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	Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu		
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	Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu Gly Val Pro Pro		

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485

490

495

Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg Ala Arg Leu Leu
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Ala Val Lys Thr Lys Leu Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg
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Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile
10 545 550 555 560

Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe Met Leu Cys Leu
565 570 575

Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu Pro Asn Arg
580 585 590

15

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 2201 amino acids

(B) TYPE: amino acid

20

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: polypeptide

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

25

(v) FRAGMENT TYPE: C-terminal fragment

(vi) IMMEDIATE SOURCE: cDNA clone pCD(38-9.4)
described by Tomei et al. 1993

(ix) FEATURE:

30

(A) NAME: NS2-NS5B Nonstructural Protein
Precursor

(C) IDENTIFICATION METHOD: Experimentally

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

Met Asp Arg Glu Met Ala Ala Ser Cys Gly Gly Ala Val Phe Val Gly
1 5 10 15

35

Leu Val Leu Leu Thr Leu Ser Pro Tyr Tyr Lys Val Phe Leu Ala Arg
20 25 30

Leu Ile Trp Trp Leu Gln Tyr Phe Thr Thr Arg Ala Glu Ala Asp Leu

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	35	40	45
	His Val Trp Ile Pro Pro Leu Asn Ala Arg Gly Gly Arg Asp Ala Ile		
	50	55	60
	Ile Leu Leu Met Cys Ala Val His Pro Glu Leu Ile Phe Asp Ile Thr		
5	65	70	75
	Lys Leu Leu Ile Ala Ile Leu Gly Pro Leu Met Val Leu Gln Ala Gly		
	85	90	95
	Ile Thr Arg Val Pro Tyr Phe Val Arg Ala Gln Gly Leu Ile His Ala		
	100	105	110
10	Cys Met Leu Val Arg Lys Val Ala Gly Gly His Tyr Val Gln Met Ala		
	115	120	125
	Phe Met Lys Leu Gly Ala Leu Thr Gly Thr Tyr Ile Tyr Asn His Leu		
	130	135	140
	Thr Pro Leu Arg Asp Trp Pro Arg Ala Gly Leu Arg Asp Leu Ala Val		
15	145	150	155
	Ala Val Glu Pro Val Val Phe Ser Asp Met Glu Thr Lys Ile Ile Thr		
	165	170	175
	Trp Gly Ala Asp Thr Ala Ala Cys Gly Asp Ile Ile Leu Gly Leu Pro		
	180	185	190
20	Val Ser Ala Arg Arg Gly Lys Glu Ile Leu Leu Gly Pro Ala Asp Ser		
	195	200	205
	Leu Glu Gly Arg Gly Leu Arg Leu Leu Ala Pro Ile Thr Ala Tyr Ser		
	210	215	220
	Gln Gln Thr Arg Gly Leu Leu Gly Cys Ile Ile Thr Ser Leu Thr Gly		
25	225	230	235
	Arg Asp Lys Asn Gln Val Glu Gly Glu Val Gln Val Val Ser Thr Ala		
	245	250	255
	Thr Gln Ser Phe Leu Ala Thr Cys Val Asn Gly Val Cys Trp Thr Val		
	260	265	270
30	Tyr His Gly Ala Gly Ser Lys Thr Leu Ala Ala Pro Lys Gly Pro Ile		
	275	280	285
	Thr Gln Met Tyr Thr Asn Val Asp Gln Asp Leu Val Gly Trp Pro Lys		
	290	295	300
	Pro Pro Gly Ala Arg Ser Leu Thr Pro Cys Thr Cys Gly Ser Ser Asp		
35	305	310	315
	Leu Tyr Leu Val Thr Arg His Ala Asp Val Ile Pro Val Arg Arg Arg		
	325	330	335

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Gly Asp Ser Arg Gly Ser Leu Leu Ser Pro Arg Pro Val Ser Tyr Leu
 340 345 350

Lys Gly Ser Ser Gly Gly Pro Leu Leu Cys Pro Phe Gly His Ala Val
 5 355 360 365

Gly Ile Phe Arg Ala Ala Val Cys Thr Arg Gly Val Ala Lys Ala Val
 370 375 380

Asp Phe Val Pro Val Glu Ser Met Glu Thr Thr Met Arg Ser Pro Val
 385 390 395 400

10 Phe Thr Asp Asn Ser Ser Pro Pro Ala Val Pro Gln Ser Phe Gln Val
 405 410 415

Ala His Leu His Ala Pro Thr Gly Ser Gly Lys Ser Thr Lys Val Pro
 420 425 430

Ala Ala Tyr Ala Ala Gln Gly Tyr Lys Val Leu Val Leu Asn Pro Ser
 15 435 440 445

Val Ala Ala Thr Leu Gly Phe Gly Ala Tyr Met Ser Lys Ala His Gly
 450 455 460

Ile Asp Pro Asn Ile Arg Thr Gly Val Arg Thr Ile Thr Thr Gly Ala
 465 470 475 480

20 Pro Val Thr Tyr Ser Thr Tyr Gly Lys Phe Leu Ala Asp Gly Gly Cys
 485 490 495

Ser Gly Gly Ala Tyr Asp Ile Ile Ile Cys Asp Glu Cys His Ser Thr
 500 505 510

Asp Ser Thr Thr Ile Leu Gly Ile Gly Thr Val Leu Asp Gln Ala Glu
 25 515 520 525

Thr Ala Gly Ala Arg Leu Val Val Leu Ala Thr Ala Thr Pro Pro Gly
 530 535 540

Ser Val Thr Val Pro His Pro Asn Ile Glu Glu Val Ala Leu Ser Asn
 545 550 555 560

30 Thr Gly Glu Ile Pro Phe Tyr Gly Lys Ala Ile Pro Ile Glu Ala Ile
 565 570 575

Arg Gly Gly Arg His Leu Ile Phe Cys His Ser Lys Lys Lys Cys Asp
 580 585 590

Glu Leu Ala Ala Lys Leu Ser Gly Leu Gly Ile Asn Ala Val Ala Tyr
 35 595 600 605

Tyr Arg Gly Leu Asp Val Ser Val Ile Pro Thr Ile Gly Asp Val Val
 610 615 620

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Val Val Ala Thr Asp Ala Leu Met Thr Gly Tyr Thr Gly Asp Phe Asp
 625 630 635 640

Ser Val Ile Asp Cys Asn Thr Cys Val Thr Gln Thr Val Asp Phe Ser
 5 645 650 655

Leu Asp Pro Thr Phe Thr Ile Glu Thr Thr Val Pro Gln Asp Ala
 660 665 670

Val Ser Arg Ser Gln Arg Arg Gly Arg Thr Gly Arg Gly Arg Arg Gly
 675 680 685

10 Ile Tyr Arg Phe Val Thr Pro Gly Glu Arg Pro Ser Gly Met Phe Asp
 690 695 700

Ser Ser Val Leu Cys Glu Cys Tyr Asp Ala Gly Cys Ala Trp Tyr Glu
 705 710 715 720

Leu Thr Pro Ala Glu Thr Ser Val Arg Leu Arg Ala Tyr Leu Asn Thr
 15 725 730 735

Pro Gly Leu Pro Val Cys Gln Asp His Leu Glu Phe Trp Glu Ser Val
 740 745 750

Phe Thr Gly Leu Thr His Ile Asp Ala His Phe Leu Ser Gln Thr Lys
 755 760 765

20 Gln Ala Gly Asp Asn Phe Pro Tyr Leu Val Ala Tyr Gln Ala Thr Val
 770 775 780

Cys Ala Arg Ala Gln Ala Pro Pro Pro Ser Trp Asp Gln Met Trp Lys
 785 790 795 800

Cys Leu Ile Arg Leu Lys Pro Thr Leu His Gly Pro Thr Pro Leu Leu
 25 805 810 815

Tyr Arg Leu Gly Ala Val Gln Asn Glu Val Thr Leu Thr His Pro Ile
 820 825 830

Thr Lys Tyr Ile Met Ala Cys Met Ser Ala Asp Leu Glu Val Val Thr
 835 840 845

30 Ser Thr Trp Val Leu Val Gly Gly Val Leu Ala Ala Leu Ala Ala Tyr
 850 855 860

Cys Leu Thr Thr Gly Ser Val Val Ile Val Gly Arg Ile Ile Leu Ser
 865 870 875 880

Gly Arg Pro Ala Ile Val Pro Asp Arg Glu Leu Leu Tyr Gln Glu Phe
 35 885 890 895

Asp Glu Met Glu Glu Cys Ala Ser His Leu Pro Tyr Ile Glu Gln Gly
 900 905 910

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Met Gln Leu Ala Glu Gln Phe Lys Gln Lys Ala Leu Gly Leu Leu Gln
 915 920 925

Thr Ala Thr Lys Gln Ala Glu Ala Ala Ala Pro Val Val Glu Ser Lys
 5 930 935 940

Trp Arg Ala Leu Glu Thr Phe Trp Ala Lys His Met Trp Asn Phe Ile
 945 950 955 960

Ser Gly Ile Gln Tyr Leu Ala Gly Leu Ser Thr Leu Pro Gly Asn Pro
 965 970 975

10 Ala Ile Ala Ser Leu Met Ala Phe Thr Ala Ser Ile Thr Ser Pro Leu
 980 985 990

Thr Thr Gln Ser Thr Leu Leu Phe Asn Ile Leu Gly Gly Trp Val Ala
 995 1000 1005

Ala Gln Leu Ala Pro Pro Ser Ala Ala Ser Ala Phe Val Gly Ala Gly
 15 1010 1015 1020

Ile Ala Gly Ala Ala Val Gly Ser Ile Gly Leu Gly Lys Val Leu Val
 1025 1030 1035 1040

Asp Ile Leu Ala Gly Tyr Gly Ala Gly Val Ala Gly Ala Leu Val Ala
 1045 1050 1055

20 Phe Lys Val Met Ser Gly Glu Met Pro Ser Thr Glu Asp Leu Val Asn
 1060 1065 1070

Leu Leu Pro Ala Ile Leu Ser Pro Gly Ala Leu Val Val Gly Val Val
 1075 1080 1085

Cys Ala Ala Ile Leu Arg Arg His Val Gly Pro Gly Glu Gly Ala Val
 25 1090 1095 1100

Gln Trp Met Asn Arg Leu Ile Ala Phe Ala Ser Arg Gly Asn His Val
 1105 1110 1115 1120

Ser Pro Thr His Tyr Val Pro Glu Ser Asp Ala Ala Ala Arg Val Thr
 1125 1130 1135

30 Gln Ile Leu Ser Ser Leu Thr Ile Thr Gln Leu Leu Lys Arg Leu His
 1140 1145 1150

Gln Trp Ile Asn Glu Asp Cys Ser Thr Pro Cys Ser Gly Ser Trp Leu
 1155 1160 1165

Arg Asp Val Trp Asp Trp Ile Cys Thr Val Leu Thr Asp Phe Lys Thr
 35 1170 1175 1180

Trp Leu Gln Ser Lys Leu Leu Pro Gln Leu Pro Gly Val Pro Phe Phe
 1185 1190 1195 1200

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Ser Cys Gln Arg Gly Tyr Lys Gly Val Trp Arg Gly Asp Gly Ile Met
 1205 1210 1215

Gln Thr Thr Cys Pro Cys Gly Ala Gln Ile Thr Gly His Val Lys Asn
 5 1220 1225 1230

Gly Ser Met Arg Ile Val Gly Pro Lys Thr Cys Ser Asn Thr Trp His
 1235 1240 1245

Gly Thr Phe Pro Ile Asn Ala Tyr Thr Thr Gly Pro Cys Thr Pro Ser
 1250 1255 1260

10 Pro Ala Pro Asn Tyr Ser Arg Ala Leu Trp Arg Val Ala Ala Glu Glu
 1265 1270 1275 1280

Tyr Val Glu Val Thr Arg Val Gly Asp Phe His Tyr Val Thr Gly Met
 1285 1290 1295

Thr Thr Asp Asn Val Lys Cys Pro Cys Gln Val Pro Ala Pro Glu Phe
 15 1300 1305 1310

Phe Ser Glu Val Asp Gly Val Arg Leu His Arg Tyr Ala Pro Ala Cys
 1315 1320 1325

Arg Pro Leu Leu Arg Glu Glu Val Thr Phe Gln Val Gly Leu Asn Gln
 1330 1335 1340

20 Tyr Leu Val Gly Ser Gln Leu Pro Cys Glu Pro Glu Pro Asp Val Ala
 1345 1350 1355 1360

Val Leu Thr Ser Met Leu Thr Asp Pro Ser His Ile Thr Ala Glu Thr
 1365 1370 1375

Ala Lys Arg Arg Leu Ala Arg Gly Ser Pro Pro Ser Leu Ala Ser Ser
 25 1380 1385 1390

Ser Ala Ser Gln Leu Ser Ala Pro Ser Leu Lys Ala Thr Cys Thr Thr
 1395 1400 1405

His His Val Ser Pro Asp Ala Asp Leu Ile Glu Ala Asn Leu Leu Trp
 1410 1415 1420

30 Arg Gln Glu Met Gly Gly Asn Ile Thr Arg Val Glu Ser Glu Asn Lys
 1425 1430 1435 1440

Val Val Val Leu Asp Ser Phe Asp Pro Leu Arg Ala Glu Glu Asp Glu
 1445 1450 1455

Arg Glu Val Ser Val Pro Ala Glu Ile Leu Arg Lys Ser Lys Lys Phe
 35 1460 1465 1470

Pro Ala Ala Met Pro Ile Trp Ala Arg Pro Asp Tyr Asn Pro Pro Leu
 1475 1480 1485

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Leu Glu Ser Trp Lys Asp Pro Asp Tyr Val Pro Pro Val Val His Gly
 1490 1495 1500

Cys Pro Leu Pro Pro Ile Lys Ala Pro Pro Ile Pro Pro Pro Arg Arg
 5 1505 1510 1515 1520

Lys Arg Thr Val Val Leu Thr Glu Ser Ser Val Ser Ser Ala Leu Ala
 1525 1530 1535

Glu Leu Ala Thr Lys Thr Phe Gly Ser Ser Glu Ser Ser Ala Val Asp
 1540 1545 1550

10 Ser Gly Thr Ala Thr Ala Leu Pro Asp Gln Ala Ser Asp Asp Gly Asp
 1555 1560 1565

Lys Gly Ser Asp Val Glu Ser Tyr Ser Ser Met Pro Pro Leu Glu Gly
 1570 1575 1580

Glu Pro Gly Asp Pro Asp Leu Ser Asp Gly Ser Trp Ser Thr Val Ser
 15 1585 1590 1595 1600

Glu Glu Ala Ser Glu Asp Val Val Cys Cys Ser Met Ser Tyr Thr Trp
 1605 1610 1615

Thr Gly Ala Leu Ile Thr Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro
 1620 1625 1630

20 Ile Asn Ala Leu Ser Asn Ser Leu Leu Arg His His Asn Met Val Tyr
 1635 1640 1645

Ala Thr Thr Ser Arg Ser Ala Gly Leu Arg Gln Lys Lys Val Thr Phe
 1650 1655 1660

Asp Arg Leu Gln Val Leu Asp Asp His Tyr Arg Asp Val Leu Lys Glu
 25 1665 1670 1675 1680

Met Lys Ala Lys Ala Ser Thr Val Lys Ala Lys Leu Leu Ser Val Glu
 1685 1690 1695

Glu Ala Cys Lys Leu Thr Pro Pro His Ser Ala Lys Ser Lys Phe Gly
 1700 1705 1710

30 Tyr Gly Ala Lys Asp Val Arg Asn Leu Ser Ser Lys Ala Val Asn His
 1715 1720 1725

Ile His Ser Val Trp Lys Asp Leu Leu Glu Asp Thr Val Thr Pro Ile
 1730 1735 1740

Asp Thr Thr Ile Met Ala Lys Asn Glu Val Phe Cys Val Gln Pro Glu
 35 1745 1750 1755 1760

Lys Gly Gly Arg Lys Pro Ala Arg Leu Ile Val Phe Pro Asp Leu Gly
 1765 1770 1775

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Val Arg Val Cys Glu Lys Met Ala Leu Tyr Asp Val Val Ser Thr Leu
 1780 1785 1790

Pro Gln Val Val Met Gly Ser Ser Tyr Gly Phe Gln Tyr Ser Pro Gly
 5 1795 1800 1805

Gln Arg Val Glu Phe Leu Val Asn Thr Trp Lys Ser Lys Lys Asn Pro
 1810 1815 1820

Met Gly Phe Ser Tyr Asp Thr Arg Cys Phe Asp Ser Thr Val Thr Glu
 1825 1830 1835 1840

10 Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Gln Cys Cys Asp Leu Ala
 1845 1850 1855

Pro Glu Ala Arg Gln Ala Ile Lys Ser Leu Thr Glu Arg Leu Tyr Ile
 1860 1865 1870

Gly Gly Pro Leu Thr Asn Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg
 15 1875 1880 1885

Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr
 1890 1895 1900

Cys Tyr Leu Lys Ala Ser Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp
 1905 1910 1915 1920

20 Cys Thr Met Leu Val Asn Gly Asp Asp Leu Val Val Ile Cys Glu Ser
 1925 1930 1935

Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg Val Phe Thr Glu Ala
 1940 1945 1950

Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr
 25 1955 1960 1965

Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val Ala His
 1970 1975 1980

Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro Thr Thr
 1985 1990 1995 2000

30 Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro Val Asn
 2005 2010 2015

Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala Pro Thr Leu Trp Ala Arg
 2020 2025 2030

Met Ile Leu Met Thr His Phe Phe Ser Ile Leu Leu Ala Gln Glu Gln
 35 2035 2040 2045

Leu Glu Lys Ala Leu Asp Cys Gln Ile Tyr Gly Ala Cys Tyr Ser Ile
 2050 2055 2060

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Glu Pro Leu Asp Leu Pro Gln Ile Ile Glu Arg Leu His Gly Leu Ser
2065 2070 2075 2080

Ala Phe Ser Leu His Ser Tyr Ser Pro Gly Glu Ile Asn Arg Val Ala
5 2085 2090 2095

Ser Cys Leu Arg Lys Leu Gly Val Pro Pro Leu Arg Val Trp Arg His
2100 2105 2110

Arg Ala Arg Ser Val Arg Ala Arg Leu Leu Ser Gln Gly Gly Arg Ala
2115 2120 2125

10 Ala Thr Cys Gly Lys Tyr Leu Phe Asn Trp Ala Val Lys Thr Lys Leu
2130 2135 2140

Lys Leu Thr Pro Ile Pro Ala Ala Ser Arg Leu Asp Leu Ser Gly Trp
2145 2150 2155 2160

Phe Val Ala Gly Tyr Ser Gly Gly Asp Ile Tyr His Ser Leu Ser Arg
15 2165 2170 2175

Ala Arg Pro Arg Trp Phe Met Leu Cys Leu Leu Leu Leu Ser Val Gly
2180 2185 2190

Val Gly Ile Tyr Leu Leu Pro Asn Arg
2195 2200

20 (3) INFORMATION FOR SEQ ID NO: 3

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 26 nucleotides

(B) TYPE: nucleic acid

25 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

30 (vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

(A) NAME: oligo a

(C) IDENTIFICATION METHOD: Polyacrylamide
35 gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3

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GCCGAGATGC CATCTTCAAA CAGTTC

26

(4) INFORMATION FOR SEQ ID NO: 4

(i) SEQUENCE CHARACTERISTICS

5 (A) LENGTH: 24 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

10 (iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

15 (A) NAME: oligo b

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4

20 GTGTACAACCA AGGTCCATAT CACC

24

(5) INFORMATION FOR SEQ ID NO: 5

(i) SEQUENCE CHARACTERISTICS

25 (A) LENGTH: 24 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

30 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

(A) NAME: oligo c

35 (C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5

GGTCTTCTG AACGGGATAT AAAC

24

- (6) INFORMATION FOR SEQ ID NO: 6:
- 5 (i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 31 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- 10 (ii) MOLECULE TYPE: synthetic DNA
(iii) HYPOTHETICAL: No
(iv) ANTISENSE: No
(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer
- 15 (ix) FEATURE:
(A) NAME: 5'-5B
(C) IDENTIFICATION METHOD: Polyacrylamide
gel
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6
- 20 AAGGATCCAT GTCAATGTCC TACACATGGA C
- 31
- (7) INFORMATION FOR SEQ ID NO: 7:
- 25 (i) SEQUENCE CHARACTERISTICS
(A) LENGTH: 36 nucleotides
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: synthetic DNA
- 30 (iii) HYPOTHETICAL: No
(iv) ANTISENSE: Yes
(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer
- 35 (ix) FEATURE:
(A) NAME: 3'-5B
(C) IDENTIFICATION METHOD: Polyacrylamide
gel

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7

AATATTGAA TTCATCGGTT GGGGAGCAGG TAGATG 36

5 (8) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 22 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

15 (ix) FEATURE:

(A) NAME: Dpr1

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8

TGGCTGGCAA GGCACACAGG CT 22

(9) INFORMATION FOR SEQ ID NO: 9

25 (i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 20 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

35 (ix) FEATURE:

(A) NAME: Dpr2

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(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9

5 AGGCAGGGTA GATCTATGTC

20

(10) INFORMATION FOR SEQ ID NO: 10

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 20 nucleotides

10 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

15 (iv) ANTISENSE: No

(vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

(A) NAME: NS5B-5' (1)

20 (C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10

TCAATGTCCT ACACATGGAC

20

25

(11) INFORMATION FOR SEQ ID NO: 11

(i) SEQUENCE CHARACTERISTICS

(A) LENGTH: 38 nucleotides

(B) TYPE: nucleic acid

30 (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

35 (vii) IMMEDIATE SOURCE: oligonucleotide
synthesizer

(ix) FEATURE:

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(A) NAME: HCVA-13

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11

5

GATCTCTAGA TCATCGGTTG GGGGAGGAGG TAGATGCC

38

(12) INFORMATION FOR SEQ ID NO: 12

(i) SEQUENCE CHARACTERISTICS

10 (A) LENGTH: 399 nucleotides

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA

15 (iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Rattus Norvegicus

(B) STRAIN : Sprague-Dawley

20 (vii) IMMEDIATE SOURCE: pT7-7 (DCoH)

(ix) FEATURE:

(A) NAME: D-RNA

(C) IDENTIFICATION METHOD: Polyacrylamide
gel

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12

GGGAGACCAC AACGGUUUCC CUCUAGAAA AUUUUUGUUU AACUUUAAGA AGGAGAUUA 60

CAUAUGGCUA GAAUUCGCGC CCUGGCUGGC AAGGCACACA GGCUGAGUGC UGAGGAACGG 120

GACCAGCUGC UGCCAAACCU GCAGGGCGUG GGGUGGAUG AACUGGAAGG CCCGAGAUGCC 180

30 AUCUUCAAAC AGUUCCAUUU UAAAGACUUC AACAGGGCUU UUGGUUCAU GACAAGAGUC 240

GCCCUUGCAGG CUGAAAAGCU GGACCACCAU CCCGAGUGGU UUAACGUGUA CAACAAGGUC 300

CAUAUCACCU UGAGCACCCA CGAAUGUGCC GGUCUUUCUG AACGGGAUUA AAACCUGGCC 360

AGCUUCAUCG AACAAAGUUGC CGUGUCUAUG ACAUAGAUC 399

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(13) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS

- (A) LENGTH: 20 nucleotides
- (B) TYPE: nucleic acid
- 5 (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: No

10 (vii) IMMEDIATE SOURCE: oligonucleotide synthesizer

(ix) FEATURE:

- (A) NAME: NS5B-up
- (C) IDENTIFICATION METHOD: Polyacrylamide gel
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13

15

TGTCAATGTC CTACACATGG

20

(14) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS

20

- (A) LENGTH: 38 nucleotides
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: synthetic DNA

25

(iii) HYPOTHETICAL: No

(iv) ANTISENSE: Yes

(vii) IMMEDIATE SOURCE: oligonucleotide synthesizer

(ix) FEATURE:

30

- (A) NAME: 3'-5B

(C) IDENTIFICATION METHOD: Polyacrylamide gel

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14

AATATTGAA TTCATCGGTT GGGGAGGCAGG TAGATG

36